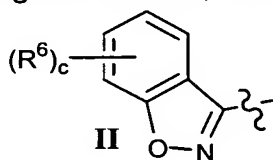


AMENDMENTS TO THE CLAIMS

1. (cancelled)

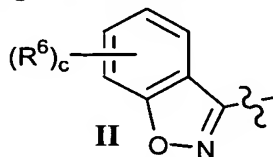
2. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R¹ is selected from:

- (A) aryl;
- (B) substituted aryl, wherein the substituents on said substituted aryl are selected from: (1) halo; or (2) alkyl; or (3) substituted alkyl;
- (C) heteroaryl;
- (D) substituted heteroaryl; or
- (E) when R¹ is taken together with X, then the moiety is



3. (currently amended) The ~~compound~~ composition of Claim 2 wherein R¹ is selected from:

- (A) phenyl;
- (B) substituted phenyl wherein the substituents on said substituted phenyl are selected from: (1) halo; (2) alkyl; (3) alkyl substituted with halo;
- (C) heteroaryl selected from: pyridyl, thienyl, pyrimidinyl, thiazolyl or pyridyl N-Oxide;
- (D) alkyl substituted thiazolyl; or
- (E) when R¹ is taken together with X, then the moiety is



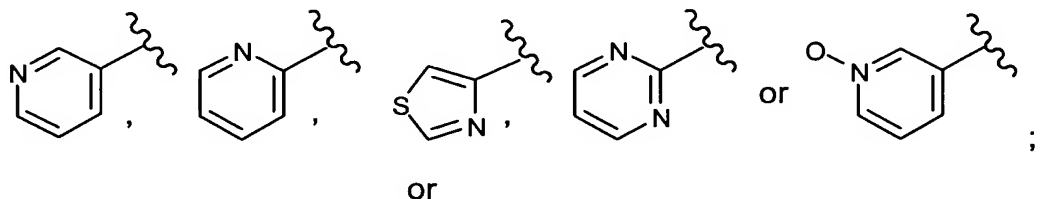
wherein c is 0 or 1, and when c is 1 then R⁶ is halo.

4. (currently amended) The ~~compound~~ composition of Claim 3 wherein R¹ is selected from:

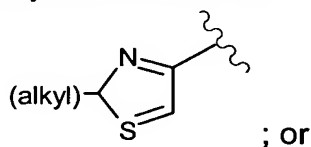
- (A) phenyl;

(B) substituted phenyl, wherein the substituents on said substituted phenyl are independently selected from: chloro, fluoro or trifluoromethyl;

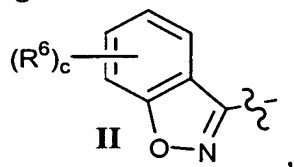
(C) heteroaryl selected from:



(D) substituted heteroaryl of the formula:



(E) when R^1 is taken together with X, then the moiety is



wherein c is 0 or 1, and when c is 1 then R^6 is fluoro.

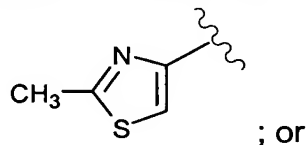
5. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R^1 is selected from:

(A) phenyl;

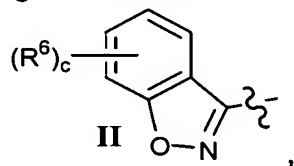
(B) substituted phenyl, wherein the substituents on said substituted phenyl are independently selected from: chloro, fluoro or trifluoromethyl;

(C) pyridyl; or

(D) substituted heteroaryl of the formula:



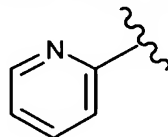
(E) when R^1 is taken together with X, then the moiety is



wherein c is 0 or 1, and when c is 1 then R^6 is fluoro.

6. (currently amended) The ~~compound~~ composition of Claim 5 wherein R^1 is pyridyl.

7. (currently amended) The ~~compound~~ composition of Claim 6 wherein R^1 is



8. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein X is $=C(NOR^3)$, and R^3 is selected from H or alkyl.

9. (currently amended) The ~~compound~~ composition of Claim 8 wherein R^3 is selected from H, methyl or ethyl.

10. (currently amended) The ~~compound~~ composition of Claim 9 wherein R^3 is methyl.

11. (currently amended) The ~~compound~~ composition of claim [[1]] 56 wherein: (1) M^2 is nitrogen; and (2) M^3 and M^4 are selected such that: (a) one is carbon and the other is nitrogen, or (b) both are nitrogen.

12. (currently amended) The ~~compound~~ composition of Claim 11 wherein M^3 is carbon, and M^4 is nitrogen.

13. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein:

n is 2;

a is 0 or 1;

b is 0 or 1;

c is 0 or 1, and when c is 1 then R^6 is halo;

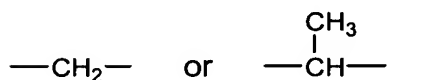
e is 1 to 5; and

p is 2.

14. (currently amended) The ~~compound~~ composition of claim [[1]] 56 wherein Y is =C(O).

15. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein Z is C₁ to C₃ alkyl.

16. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein Z is

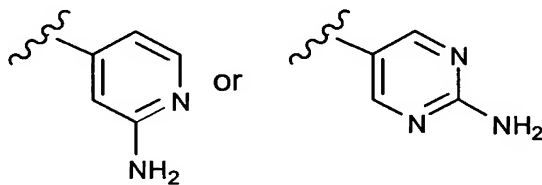


17. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R² is a six membered heteroaryl ring.

18. (currently amended) The ~~compound~~ composition of Claim 17 wherein R² is selected from pyridyl, pyridyl substituted with —NR⁴R⁵, pyrimidinyl, or pyrimidinyl substituted with —NR⁴R⁵.

19. (currently amended) The ~~compound~~ composition of Claim 18 wherein R² is pyridyl substituted with —NH₂, or pyrimidinyl substituted with —NH₂.

20. (currently amended) The ~~compound~~ composition of Claim 19 wherein R² is



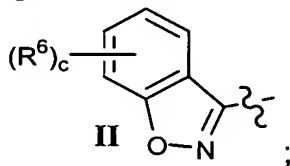
21. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R⁴ is H or lower alkyl; R⁵ is H, C₁ to C₆alkyl, or —C(O)R⁴; R¹² is alkyl, hydroxy or fluoro; and R¹³ is alkyl, hydroxy or fluoro.

22. (currently amended) The ~~compound~~ composition of Claim 21 wherein R^4 is H or methyl; R^5 is H or methyl; R^{12} is hydroxy or fluoro; and R^{13} is hydroxy or fluoro.

23. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein:

(1) R^1 is selected from:

- (A) aryl;
- (B) substituted aryl, wherein the substituents on said substituted aryl are selected from: (1) halo; or (2) alkyl; or (3) substituted alkyl;
- (C) heteroaryl; or
- (D) substituted heteroaryl; or
- (E) when R^1 is taken together with X, then the moiety is

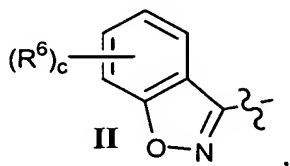


- (2) X is $=C(NOR^3)$;
- (3) R^3 is selected from H or alkyl;
- (4) M^2 is nitrogen;
- (5) Y is $=C(O)$;
- (6) M^3 and M^4 are selected such that: (1) one is carbon and the other is nitrogen, or (2) both are nitrogen;
- (7) Z is C_1 to C_3 alkyl; and
- (8) R^2 is a six membered heteroaryl ring.

24. (currently amended) The ~~compound~~ composition of Claim 23 wherein:

- (1) R^1 is selected from:
 - (A) phenyl;
 - (B) substituted phenyl wherein the substituents on said substituted phenyl are selected from: (1) halo; (2) alkyl; (3) alkyl substituted with halo;
 - (C) heteroaryl selected from: pyridyl, thienyl, pyrimidinyl, thiazolyl or pyridyl N-Oxide; or
 - (D) alkyl substituted thiazolyl; or

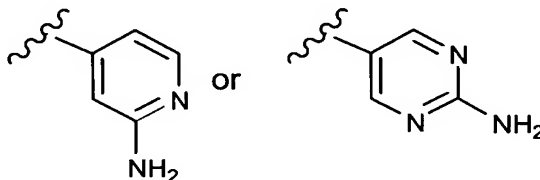
(E) when R^1 is taken together with X, then the moiety is



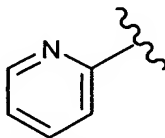
wherein c is 0 or 1, and when c is 1 then R^6 is halo;

- (2) R^3 is selected from H, methyl or ethyl;
- (3) n is 2,
- (4) a is 0 or 1,
- (5) b is 0 or 1,
- (6) c is 0 or 1 and when c is 1 then R^6 is halo,
- (7) e is 1 to 5,
- (8) p is 2,
- (9) R^4 is H or lower alkyl,
- (10) R^5 is H, C_1 to C_6 alkyl, or $-C(O)R^4$;
- (11) R^{12} is alkyl, hydroxy or fluoro, and
- (12) R^{13} is alkyl, hydroxy or fluoro.

25. (currently amended) The ~~compound~~ composition of Claim 24 wherein R^2 is



R^1 is



M^2 is nitrogen, M^3 is carbon, and M^4 is nitrogen.

26 to 43. (cancelled)

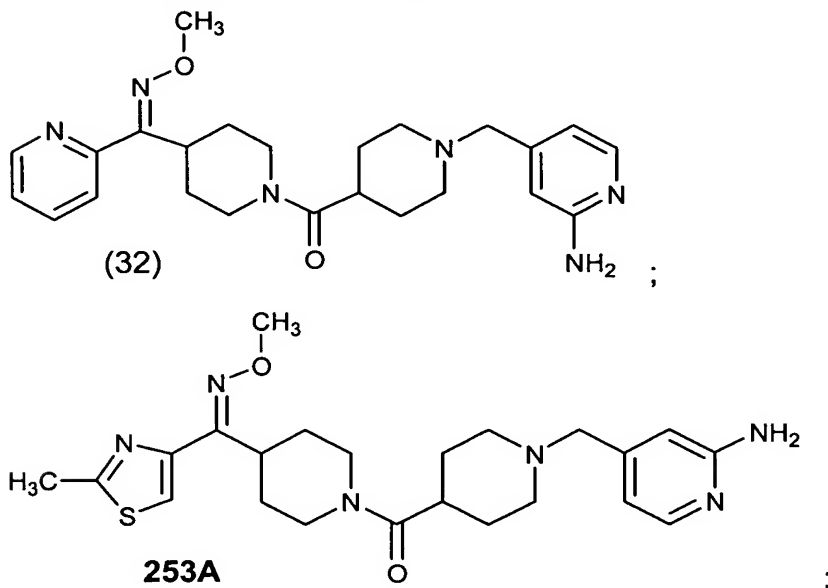
44. (currently amended) The method of Claim [[43]] 57 wherein said H₁ receptor antagonist is selected from: astemizole, azatadine, azelastine, acrivastine, brompheniramine, cetirizine, chlorpheniramine, clemastine, cyclizine, carebastine, cyproheptadine, carbinoxamine, descarboethoxyloratadine, diphenhydramine, doxylamine, dimethindene, ebastine, epinastine, efletirizine, fexofenadine, hydroxyzine, ketotifen, loratadine, levocabastine, meclizine, mizolastine, mequitazine, mianserin, noberastine, norastemizole, picumast, pyrilamine, promethazine, terfenadine, tripelennamine, temelastine, trimeprazine or triprolidine.

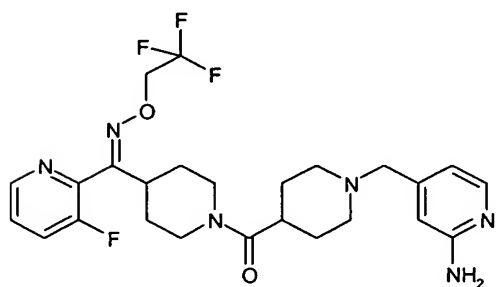
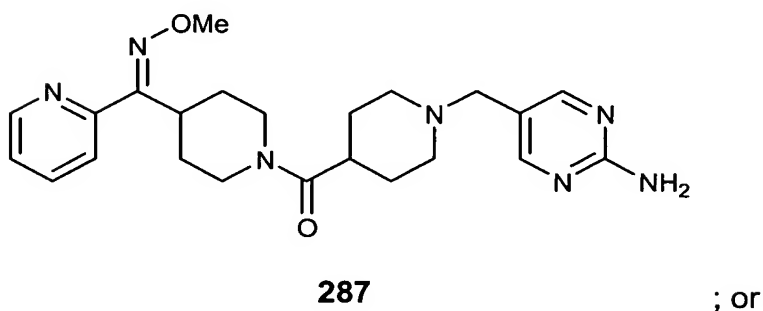
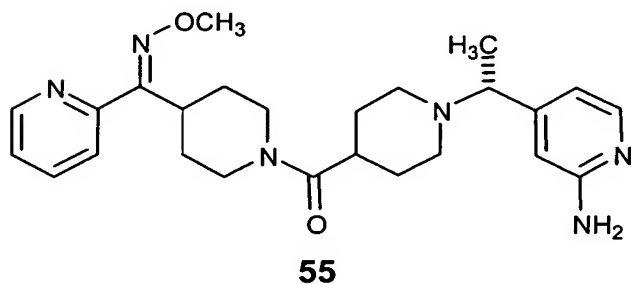
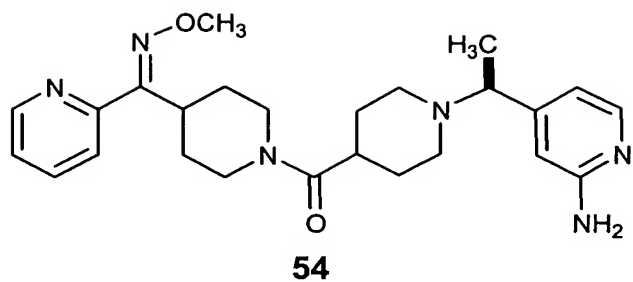
45. (original) The method of Claim 44 wherein said H₁ receptor antagonist is selected from: loratadine, descarboethoxyloratadine, fexofenadine or cetirizine.

46. (original) The method of Claim 45 wherein said H₁ receptor antagonist is selected from: loratadine or descarboethoxyloratadine.

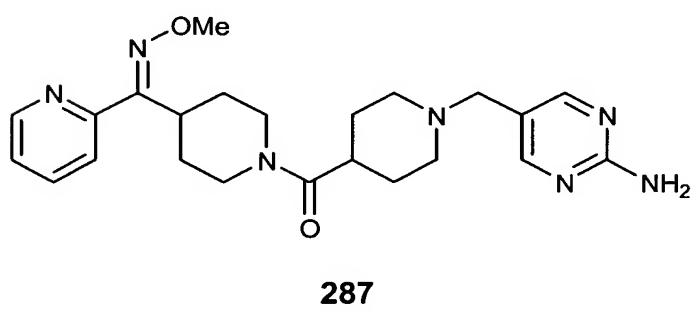
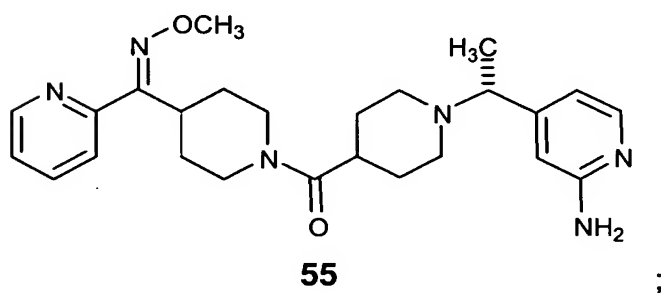
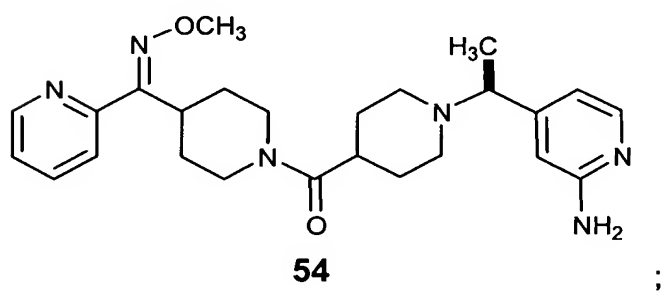
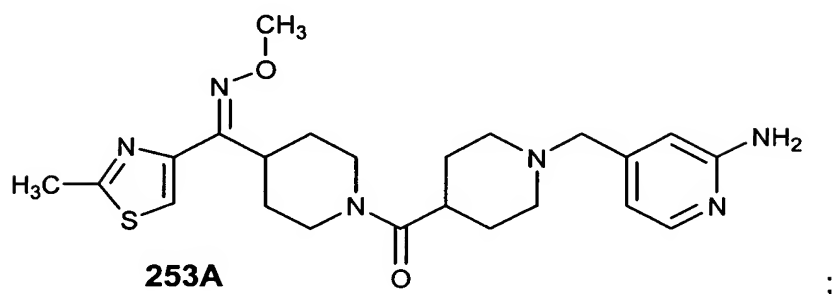
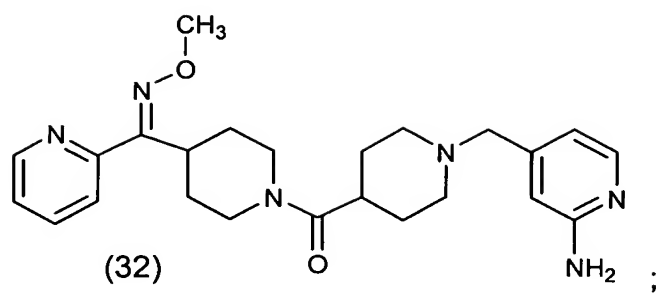
47 to 50. (cancelled)

51. (currently amended) A pharmaceutical composition ~~comprising an effective amount of a compound of Claim 1 of Claim 56, and an effective amount of H₁ receptor antagonist, and a pharmaceutically effective carrier,~~ wherein said compound of Claim 1 formula I is selected from:

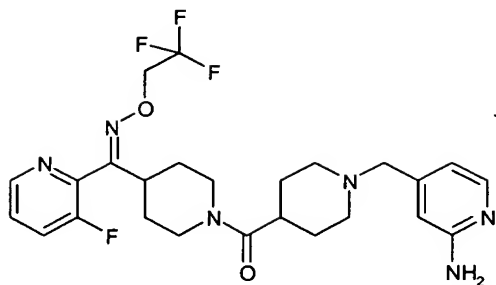




52. (currently amended) A method of treating: ~~allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of Claim 1 in combination with an effective amount of an H₁ receptor antagonist, Claim 57~~ wherein said compound of Claim 1 formula I is selected from:



; or

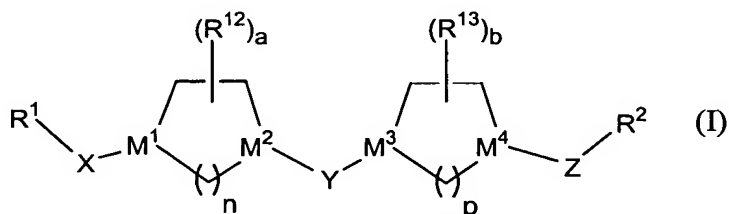


53. (original) The method of Claim 52 wherein said H_1 receptor antagonist is selected from: astemizole, azatadine, azelastine, acrivastine, brompheniramine, cetirizine, chlorpheniramine, clemastine, cyclizine, carebastine, cyproheptadine, carbinoxamine, descarboethoxyloratadine, diphenhydramine, doxylamine, dimethindene, ebastine, epinastine, efletirizine, fexofenadine, hydroxyzine, ketotifen, loratadine, levocabastine, meclizine, mizolastine, mequitazine, mianserin, noberastine, norastemizole, picumast, pyrilamine, promethazine, terfenadine, tripeleminamine, temelastine, trimeprazine or triprolidine.

54. (original) The method of Claim 53 wherein said H_1 receptor antagonist is selected from: loratadine, descarboethoxyloratadine, fexofenadine or cetirizine.

55. (original) The method of Claim 54 wherein said H_1 receptor antagonist is selected from: loratadine or descarboethoxyloratadine.

56. (new) A pharmaceutical composition comprising an effective amount of a compound of the formula I:



or a pharmaceutically acceptable salt or solvate thereof, wherein:

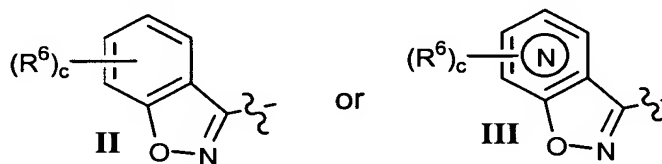
(1) R^1 is selected from:

- (a) aryl;
- (b) heteroaryl;

- (c) heterocycloalkyl
- (d) alkyl;
- (e) cycloalkyl; or
- (f) alkylaryl;

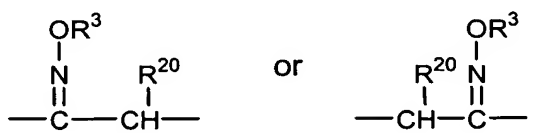
wherein said R^1 groups are optionally substituted with 1 to 4 substituents independently selected from:

- (1) halogen;
 - (2) hydroxyl;
 - (3) lower alkoxy;
 - (4) $-CF_3$;
 - (5) CF_3O- ;
 - (6) $-NR^4R^5$;
 - (7) phenyl;
 - (8) $-NO_2$;
 - (9) $-CO_2R^4$;
 - (10) $-CON(R^4)_2$ wherein each R^4 is the same or different;
 - (11) $-S(O)_mN(R^{20})_2$ wherein each R^{20} is the same or different H or alkyl group;
 - (12) $-CN$; or
 - (13) alkyl; or
- (2) R^1 and X taken together form a group selected from:

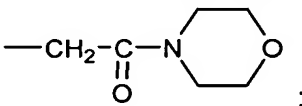


wherein \textcircled{N} represents a nitrogen atom located at one of the 4 non-fused positions of the ring;

- (3) X is selected from: $=C(O)$, $=C(NOR^3)$, $=C(NNR^4R^5)$,



- (4) M^1 is carbon;
- (5) M^2 is selected from C or N;

- (6) M^3 and M^4 are independently selected from C or N;
- (7) Y is selected from: is $-\text{CH}_2-$, $=\text{C}(\text{O})$, $=\text{C}(\text{NOR}^{20})$ (wherein R^{20} is as defined above), or $=\text{C}(\text{S})$;
- (8) Z is a $\text{C}_1 - \text{C}_6$ alkyl group;
- (9) R^2 is a five or six-membered heteroaryl ring, said six-membered heteroaryl ring comprising 1 or 2 nitrogen atoms with the remaining ring atoms being carbon, and said five-membered heteroaryl ring containing 1 or 2 heteroatoms selected from: nitrogen, oxygen, or sulfur with the remaining ring atoms being carbon; said five or six membered heteroaryl rings being optionally substituted with 1 to 3 substituents independently selected from: halogen, hydroxyl, lower alkyl, lower alkoxy, $-\text{CF}_3$, $\text{CF}_3\text{O}-$, $-\text{NR}^4\text{R}^5$, phenyl, $-\text{NO}_2$, $-\text{CO}_2\text{R}^4$, $-\text{CON}(\text{R}^4)_2$ wherein each R^4 is the same or different, $-\text{CH}_2\text{NR}^4\text{R}^5$, $-(\text{N})\text{C}(\text{NR}^4\text{R}^5)_2$, or $-\text{CN}$;
- (10) R^3 is selected from:
- (a) hydrogen;
 - (b) $\text{C}_1 - \text{C}_6$ alkyl;
 - (c) aryl;
 - (d) heteroaryl;
 - (e) heterocycloalkyl;
 - (f) arylalkyl;
 - (g) $-(\text{CH}_2)_e-\text{C}(\text{O})\text{N}(\text{R}^4)_2$ wherein each R^4 is the same or different,
 - (h) $-(\text{CH}_2)_e-\text{C}(\text{O})\text{OR}^4$;
 - (i) $-(\text{CH}_2)_e-\text{C}(\text{O})\text{R}^{30}$ wherein R^{30} is a heterocycloalkyl group, or
- 
- (j) $-\text{CF}_3$; or
 - (k) $-\text{CH}_2\text{CF}_3$;

wherein said aryl, heteroaryl, heterocycloalkyl, and the aryl portion of said arylalkyl are optionally substituted with 1 to 3 substituents selected from: halogen, $-\text{OH}$, $-\text{OCF}_3$, $-\text{CF}_3$, $-\text{CN}$, $-\text{N}(\text{R}^{45})_2$, $-\text{CO}_2\text{R}^{45}$, or $-\text{C}(\text{O})\text{N}(\text{R}^{45})_2$, wherein each R^{45} is independently selected from: H, alkyl, arylalkyl, or aryl where said aryl moiety is substituted with 1 to 3 substituents independently selected from $-\text{CF}_3$, $-\text{OH}$, halogen, alkyl, $-\text{NO}_2$, or $-\text{CN}$;

(11) R^4 is selected from: hydrogen, $C_1 - C_6$ alkyl, aryl, alkylaryl, said aryl and alkylaryl groups being optionally substituted with 1 to 3 substituents selected from: halogen, $-CF_3$, $-OCF_3$, $-OH$, $-N(R^{45})_2$, $-CO_2R^{45}$, $-C(O)N(R^{45})_2$, or $-CN$; wherein R^{45} is as defined above;

(12) R^5 is selected from: hydrogen, $C_1 - C_6$ alkyl, $-C(O)R^4$, $-C(O)_2R^4$, or $-C(O)N(R^4)_2$ wherein each R^4 is independently selected, and R^4 is as defined above;

(13) or R^4 and R^5 taken together with the nitrogen atom to which they are bound forms a five or six membered heterocycloalkyl ring;

(14) R^6 is selected from: alkyl, aryl, alkylaryl, halogen, hydroxyl, lower alkoxy, $-CF_3$, CF_3O- , $-NR^4R^5$, $-NO_2$, $-CO_2R^4$, $-CON(R^4)_2$ wherein each R^4 is the same or different, or $-CN$;

(15) R^{12} is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(16) R^{13} is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(17) a is 0 to 2;

(18) b is 0 to 2;

(19) c is 0 to 2;

(20) e is 0 to 5;

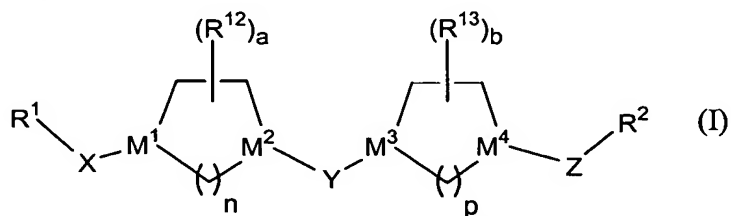
(21) m is 1 or 2;

(22) n is 1, 2 or 3; and

(23) p is 1, 2 or 3, with the proviso that when M^3 and M^4 are both nitrogen, then p is 2 or 3;

and an effective amount of H_1 receptor antagonist, and a pharmaceutically effective carrier.

57. (new) A method of treating: allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of formula I:



or a pharmaceutically acceptable salt or solvate thereof, wherein:

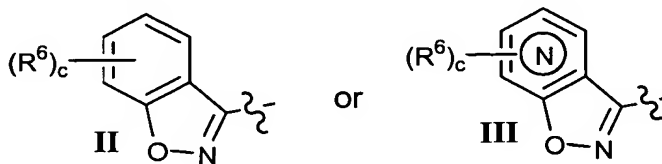
(1) R^1 is selected from:

- (a) aryl;
- (b) heteroaryl;
- (c) heterocycloalkyl
- (d) alkyl;
- (e) cycloalkyl; or
- (f) alkylaryl;

wherein said R^1 groups are optionally substituted with 1 to 4 substituents independently selected from:

- (1) halogen;
- (2) hydroxyl;
- (3) lower alkoxy;
- (4) $-CF_3$;
- (5) CF_3O- ;
- (6) $-NR^4R^5$;
- (7) phenyl;
- (8) $-NO_2$;
- (9) $-CO_2R^4$;
- (10) $-CON(R^4)_2$ wherein each R^4 is the same or different;
- (11) $-S(O)_mN(R^{20})_2$ wherein each R^{20} is the same or different H or alkyl group;
- (12) $-CN$; or
- (13) alkyl; or

(2) R^1 and X taken together form a group selected from:



wherein \textcircled{N} represents a nitrogen atom located at one of the 4 non-fused positions of the ring;

(3) X is selected from: $=C(O)$, $=C(NOR^3)$, $=C(NNR^4R^5)$,



- (4) M^1 is carbon;
- (5) M^2 is selected from C or N;
- (6) M^3 and M^4 are independently selected from C or N;
- (7) Y is selected from: is $-\text{CH}_2-$, $=\text{C}(\text{O})$, $=\text{C}(\text{NOR}^{20})$ (wherein R^{20} is as defined above), or $=\text{C}(\text{S})$;
- (8) Z is a $\text{C}_1 - \text{C}_6$ alkyl group;
- (9) R^2 is a five or six-membered heteroaryl ring, said six-membered heteroaryl ring comprising 1 or 2 nitrogen atoms with the remaining ring atoms being carbon, and said five-membered heteroaryl ring containing 1 or 2 heteroatoms selected from: nitrogen, oxygen, or sulfur with the remaining ring atoms being carbon; said five or six membered heteroaryl rings being optionally substituted with 1 to 3 substituents independently selected from: halogen, hydroxyl, lower alkyl, lower alkoxy, $-\text{CF}_3$, $\text{CF}_3\text{O}-$, $-\text{NR}^4\text{R}^5$, phenyl, $-\text{NO}_2$, $-\text{CO}_2\text{R}^4$, $-\text{CON}(\text{R}^4)_2$ wherein each R^4 is the same or different, $-\text{CH}_2\text{NR}^4\text{R}^5$, $-(\text{N})\text{C}(\text{NR}^4\text{R}^5)_2$, or $-\text{CN}$;
- (10) R^3 is selected from:
- hydrogen;
 - $\text{C}_1 - \text{C}_6$ alkyl;
 - aryl;
 - heteroaryl;
 - heterocycloalkyl;
 - arylalkyl;
 - $-(\text{CH}_2)_e-\text{C}(\text{O})\text{N}(\text{R}^4)_2$ wherein each R^4 is the same or different,
 - $-(\text{CH}_2)_e-\text{C}(\text{O})\text{OR}^4$;
 - $-(\text{CH}_2)_e-\text{C}(\text{O})\text{R}^{30}$ wherein R^{30} is a heterocycloalkyl group, or
- $$\begin{array}{c}
 \text{---CH}_2\text{---C---} \\
 || \\
 \text{O}
 \end{array}
 \begin{array}{c}
 \diagup \quad \diagdown \\
 \text{N} \quad \text{O} \\
 \diagdown \quad \diagup \\
 \text{---} \quad \text{---}
 \end{array}
 ;$$
- $-\text{CF}_3$; or
 - $-\text{CH}_2\text{CF}_3$;

wherein said aryl, heteroaryl, heterocycloalkyl, and the aryl portion of said arylalkyl are optionally substituted with 1 to 3 substituents selected from:

halogen, -OH, -OCF₃, -CF₃, -CN, -N(R⁴⁵)₂, -CO₂R⁴⁵, or -C(O)N(R⁴⁵)₂, wherein each R⁴⁵ is independently selected from: H, alkyl, alkylaryl, or aryl wherein said aryl moiety is substituted with 1 to 3 substituents independently selected from -CF₃, -OH, halogen, alkyl, -NO₂, or -CN;

(11) R⁴ is selected from: hydrogen, C₁ – C₆ alkyl, aryl, alkylaryl, said aryl and alkylaryl groups being optionally substituted with 1 to 3 substituents selected from: halogen, -CF₃, -OCF₃, -OH, -N(R⁴⁵)₂, -CO₂R⁴⁵, -C(O)N(R⁴⁵)₂, or -CN; wherein R⁴⁵ is as defined above;

(12) R⁵ is selected from: hydrogen, C₁ – C₆ alkyl, -C(O)R⁴, -C(O)₂R⁴, or -C(O)N(R⁴)₂ wherein each R⁴ is independently selected, and R⁴ is as defined above;

(13) or R⁴ and R⁵ taken together with the nitrogen atom to which they are bound forms a five or six membered heterocycloalkyl ring;

(14) R⁶ is selected from: alkyl, aryl, alkylaryl, halogen, hydroxyl, lower alkoxy, -CF₃, CF₃O-, -NR⁴R⁵, -NO₂, -CO₂R⁴, -CON(R⁴)₂ wherein each R⁴ is the same or different, or -CN;

(15) R¹² is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(16) R¹³ is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(17) a is 0 to 2;

(18) b is 0 to 2;

(19) c is 0 to 2;

(20) e is 0 to 5;

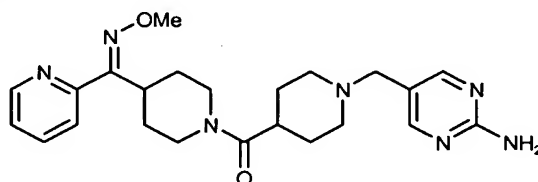
(21) m is 1 or 2;

(22) n is 1, 2 or 3; and

(23) p is 1, 2 or 3, with the proviso that when M³ and M⁴ are both nitrogen, then p is 2 or 3;

in combination with an effective amount of an H₁ receptor antagonist.

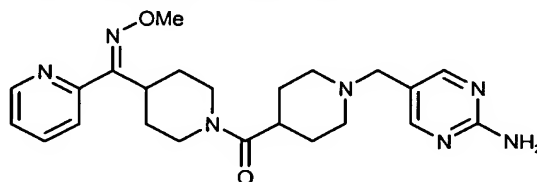
58. (new) A pharmaceutical composition comprising an effective amount of a compound of the formula



and an effective amount of H₁ receptor antagonist, and a pharmaceutically effective carrier.

59. (new) The composition of claim 58 wherein the H₁ receptor antagonist is selected from loratadine or descarboethoxyloratadine.

60. (new) A method of treating: allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of the formula



in combination with an effective amount of an H₁ receptor antagonist.

61. (new) The method of claim 60 wherein the H₁ receptor antagonist is selected from loratadine or descarboethoxyloratadine.